

REMARKS

Applicant requests reconsideration of the present application in view of the reasons that follow.

I. STATUS OF CLAIMS

Claims 1-16, 18-20, 22-29 and 31 have been cancelled and claim 17 has been amended to conform the claims to the previously issued Restriction Requirement. Applicant specifically reserves the right to pursue the cancelled subject matter in one or more continuing applications. Claims 21 and 30 also have been amended. Thus, after amending the claims as directed above, claims 17, 21 and 30 will be pending in this case.

II. OBJECTIONS

The examiner objects to pages 14, 16 and 17 for improperly referencing nucleic acid sequences. Applicant believes the amendments entered above obviate the objection.

The examiner also objects to page 19 for containing a hyperlink. Applicant has replaced the hyperlink with a simple address. Applicant notes in this regard that the address is presently underlined to illustrate that it is added language but that the address is not a URL. Thus, applicant believes the amendments obviate the objection.

The examiner also objects to pages 19-20 for containing uncapitalized trademarks. Applicant believes the amendments entered above obviate the objection.

Finally, the examiner objects to claim 30 for referencing a "medicament." Applicant believes the amendments entered above obviate the objection.

III. REJECTIONS UNDER 35 U.S.C. §§ 112, ¶2 & 101

The examiner rejects claims 17, 19-21 and 26-30 under 35 U.S.C. § 112, ¶2 and 35 U.S.C. § 101 for allegedly not "setting forth any steps". Applicant has added an administration step to the claims and believe the amendment obviates the rejections.

IV. REJECTIONS UNDER 35 U.S.C. § 112 ¶1

The examiner also rejects claims 17, 19-21 and 26-30 under 35 U.S.C. § 112, ¶1 for allegedly failing to comply with the written description requirement. In particular, the examiner asserts that “the elected invention encompasses methods comprising antisense oligonucleotides and siRNAs that target genes other than TWEAK” and that “[t]he structure of TWEAK modulators encompassed by the claims is not [sufficiently] described...such that one of skill would recognize that Applicant had possession of the invention at the time of filing.” Office Action, pg. 6.

Applicant respectfully disagrees. To advance prosecution in this case, however, applicant has directed the claims to methods for the treatment or prophylaxis of stroke comprising administering an antisense nucleic acid sequence or a siRNA that is complementary to TWEAK mRNA. Nevertheless, applicant reserves the right to pursue the cancelled subject matter in one or more continuing applications.

V. REJECTIONS UNDER 35 U.S.C. § 102

The examiner rejects claims 17, 19, 21 and 26-30 under 35 U.S.C. § 102(b) for allegedly being anticipated by Wiley (U.S. 2002/0041876). Applicant respectfully traverses the rejection.

In levying the rejection, the examiner asserts that “Wiley teaches methods of treating and preventing angiogenic-dependent diseases, such as ischaemia of the brain (stroke) by administering an antisense nucleic acid targeted to TWEAK.” Office Action, pg. 9. The assertion is factually erroneous, however.

In fact, the cited sections of Wiley purport to provide methods and compositions for either inhibiting or promoting angiogenesis via administering one of a variety of TWEAKR antagonists so as to treat a myriad of diseases. Wiley suggests that polypeptides comprising a fragment of TWEAKR extracellular domain, soluble TWEAKR multimers, antibodies that bind to the TWEAKR extracellular domain, antibodies against TWEAK, antisense nucleic acids, ribozymes, muteins, aptamers, and small molecules directed against TWEAKR or against TWEAK can be used as TWEAKR antagonists. See U.S. 2002/0041876, ¶[0107].

As for diseases, Wiley muses that TWEAKR antagonists can be used to treat such diseases as ocular disorders such as eye diseases characterized by ocular neovascularization including diabetic retinopathy, retinopathy of prematurity, neovascular glaucoma, retinoblastoma, retrobulbar fibroplasia, rubeosis, uveitis, macular degeneration, and corneal graft neovascularization, inflammatory diseases such as arthritis, rheumatism, and psoriasis, ocular tumors, diseases associated with choroidal or iris neovascularization, malignant and metastatic conditions such as solid tumors, benign tumors and preneoplastic conditions, myocardial angiogenesis, hemophilic joints, scleroderma, vascular adhesions, atherosclerotic plaque neovascularization, telangiectasia, wound granulation, coronary or peripheral atherosclerosis and ischemia of any tissue or organ, including the heart, liver, brain, and the like. *Id.* at ¶¶ [0102] to [0106].

Thus, far from teaching the specific combinations recited in the claimed method, Wiley merely provides a series of lists identifying a number of classes of compounds that might be useful to modulate a number of targets so as to potentially treat a plethora of disease states. Such a broad and hollow disclosure cannot anticipate the specific methods presently claimed. See, e.g. *In Re Petering*, 301 F.2d 676 (CCPA 1962).

Furthermore, in order to be anticipating, a prior art reference must be enabling so that the claimed subject matter may be made or used by one skilled in the art. *Impax Laboratories, Inc. v. Aventis Pharmaceuticals Inc.*, 468 F.3d 1366, 1381 (Fed. Cir. 2006). Here, the cited material fails to show that any of the hypothetical combinations would yield a successful therapy, let alone the specific combination of therapeutic agent, target and treatment presently claimed. Moreover, the cited material does not even hint at how TWEAKR antagonists might be used to “promote angiogenesis”.

Accordingly, Wiley cannot anticipate the claimed invention. Applicant requests, therefore, that the rejection be withdrawn.

VI. REJECTIONS UNDER 35 U.S.C. § 103

The examiner also rejects claims 17, 19-21 and 26-30 under 35 U.S.C. § 103(a) for allegedly being unpatentable over Wiley in view of Bass. Applicant respectfully traverses the rejection.

Wiley's disclosure is described above. Bass, cited for allegedly teaching that RNAi mediated siRNA is more robust than antisense techniques, fails to rectify the deficiencies of the primary reference. Thus, no combination of teachings from the cited art could have pointed the skilled artisan to a method for the treatment or prophylaxis of stroke comprising administering to a patient in need thereof a substance that inhibits the expression of TWEAK in neural cells, wherein the substance is an antisense nucleic acid sequence or a siRNA complementary to TWEAK mRNA. For this reason alone, the obviousness rejection must be withdrawn.

Further evincing the erroneous nature of the rejection is an absence from the record of a reasonable expectation of success in reaching the claimed invention. As noted above, the cited material fails to show that any of the hypothetical combinations would yield a successful therapy, let alone the specific combination of therapeutic agent, target and treatment presently claimed. Beyond an absence of data, the specification advances opposing theories of activity. On the one hand, Wiley asserts that TWEAKR antagonists can be used to "inhibit angiogenesis" and thereby be used to treat such maladies as "ocular disorders, malignant and metastatic conditions, and inflammatory diseases." *See U.S. 2002/0041876, ¶ [0101].* On the other hand, Wiley asserts that TWEAKR antagonists can be used to "promote angiogenesis", which might facilitate their use in treating "coronary or peripheral atherosclerosis and ischemia". *See U.S. 2002/0041876, ¶ [0106].* In the absence of data or an explanation resolving the explicit contradiction, a skilled person reviewing the cited material could not derive a reasonable expectation for success in achieving the claimed invention.

Accordingly, a prima facie case of obviousness has not been established. Applicant requests, therefore, that the rejection be withdrawn.

Applicant believes that the present application is now in condition for allowance.
Favorable reconsideration of the application is requested.

The examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extension of time is needed for timely acceptance of papers submitted herewith, applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extension fee to Deposit Account No. 19-0741.

Respectfully submitted,

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